DETAILED ACTION

Election/Restrictions

Claims 59, 66, 68-69, and 72-75 are currently pending in the application.

Applicant's election of Group IX (i.e. method of treating pain) and cyclopropane carboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide and complex regional pain syndrome as the elected species in the reply filed on 04/03/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Thus, the requirement is deemed proper and is therefore made FINAL.

Claim 66 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group and species, there being no allowable generic or linking claim.

Objections

The abstract of the disclosure is objected to because it contains legal phraseology such as "comprise" in line 2. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claims 68 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 68 is dependent on claim 66 which is now withdrawn. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59, 68-69 and 72-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of acute pain or complex regional pain syndrome, does not reasonably provide enablement for the treatment of all pain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of treating pain, which comprises administering to a patient in need thereof a therapeutically effective amount of

cyclopropane carboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide, or a pharmaceutically acceptable salt, solvate or stereoisomer thereof. The instant specification fails to provide information that would allow the skilled artisan to practice the treatment of all pain known in the art such as visceral pain or bone cancer pain.

[In re Sichert, 196 USPQ 209 (CCPA 1977)]

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to a method of treating pain, which comprises administering to a patient in need thereof a therapeutically effective amount of cyclopropane carboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide, or a pharmaceutically acceptable salt, solvate or stereoisomer thereof. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites that applicant does not particularly teach a method of treating visceral pain or pain due to cancer which are often unresponsive to drug treatments.

2. The breadth of the claims

The claims are thus very broad insofar as they recite the "treatment of all types of pain". While such "treatment" might theoretically be possible for some selective cytokine inhibitors, as a practical matter it is nearly impossible to achieve a treatment for all possible pain with the same compound.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for all types of pain. No reasonably specific guidance is provided concerning useful therapeutic protocols for all types of pain, other than acute pain, chronic pain, and complex regional pain syndrome. The latter is corroborated by the working examples on pages 75-78.

The instant disclosure provides no evidence to suggest that this unique activity of the selective cytokine inhibitor can be extrapolated to all types of pain, and thus does not meet the "how to use" prong of 35 USC 112, first paragraph with regard thereto.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the

instantly claimed selective cytokine inhibitor could be predictably used for the treatments of all types of pain as inferred by the claims and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

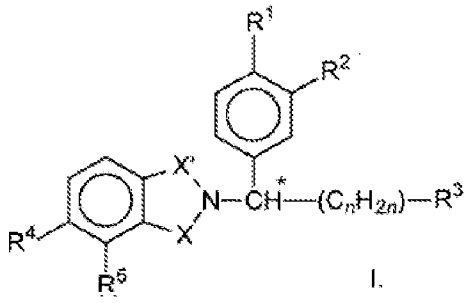
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 59, 68-69, and 72-75 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Man et al. (WO 01/34606 A1) in view of Huygen et al. (Research Communications. Mediators of Inflammation. 2002, Vol. 11, pgs. 47-51).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Man et al. teaches a method useful in the treatment of disease states mediated by Tumor Necrosis Factor-alpha (TNF-α) comprising administering isoindoline compounds (see abstract). Man et al. further teaches that the compounds of the invention inhibit TNF-α and are particularly useful in the treatment of inflammatory diseases (see pg. 1, lines 7-11) given that TNF-α is a mediator of tissue injury (see pg. 5, lines 25-28). Therefore, decreasing TNF-α levels constitute a viable therapeutic strategy for the treatment of inflammatory diseases (see pg. 9, lines 18-20). In particular, teaches the elected species cyclopropane carboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide with formula I,



I.

Where R1 and R2 are alkoxy of C1-C4; one of X and X' is C=O and the other X or X' is CH2; n has a value of 1, R3 is SO2Y with Y being an alkyl of 1 to 6 carbon

atoms; R4 and R5 is hydrogen and the other is R6NR7-CzH2z in which z is 0; R7 is H and R6 is N-substituted carbamoyl in which the substituents is cycloalkyl of 3 to 18 carbon atoms (see pgs. 10-11). Additionally, Man et al. teaches the salt compounds or administration of pure isomers of the aforementioned compounds which can be administered orally in the form of tablets or capsules (instant claims 72 and 74-75; pg. 22, lines 3-6).

Man et al. does not particularly teach a method of treating complex regional pain syndrome of type 1 or II or administration of the aforementioned compound before, during, or after surgery, psychological or physical therapy.

Huygen et al. teaches that complex regional pain syndrome type 1 (CRPS1) is a disease characterized by spontaneous pain, allodynia and hyperalgesia (instant claims 68-69; see pg. 47, Introduction section, left col.). Importantly, Huygen et al. teaches that CRPS1 involves activation of the immune system and subsequent involvement of neurogenic inflammation (see pg. 47, Introduction Section, right col.). Huygen et al. further suggests that substance P may be involved and this could consequently lead to the release of IL-1ß and TNF-α and subsequent inflammation observed in CRPS1 (see pg. 47, right col. and pg. 48. left col. Introduction Section). Importantly, Huygen et al. reveals that TNF-α was significantly elevated in CRPS1 and suggests the use of pharmacological intervention for decreasing inflammation mediators and for providing beneficial effects on disease activity (see pg. 50, table 3, Results section, and Discussion section, last paragraph and pg. 51). Huygen et al. also teaches that some

of the patients involved in the study acquired CRPS 1 as a result of surgery suggesting that any treatment of CRPS1 will necessarily be administered after surgery (instant claim 73; see pg. 48, table 1).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to administer cyclopropane carboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide to treat complex regional pain syndrome type 1 since Man et al. teaches that the aforementioned compound can be used in disease states mediated by TNF-α and given that Huygen et al. teaches that CRPS1 involved high levels of TNF-α and favors the use of inflammatory mediator antagonists or inhibitors in treating CRPS1. Given that Man et al. teaches a method of treating disease states mediated by TNF-α by administering isoindoline compounds, and Huygen et al. teaches the use of inflammatory mediator antagonists or inhibitors in treating CRPS1, a disease characterized by high levels of TNF-α, one of ordinary skill would have been motivated to treat complex regional pain syndrome type 1 as taught by Huygen et al. with the compound of Man et al. with the reasonable expectation of providing a method that is efficient in treating CRPS1 and a method effective in reducing the levels of TNF-α.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

05/30/2008

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617